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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/537,731	04/17/2006	Aldo Salimbeni	309,992	7958

38137 7590 10/25/2010

ABELMAN, FRAYNE & SCHWAB
666 THIRD AVENUE, 10TH FLOOR
NEW YORK, NY 10017

EXAMINER	
HA, JULIE	

ART UNIT	PAPER NUMBER
1654	

MAIL DATE	DELIVERY MODE
10/25/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/537,731	SALIMBENI ET AL.	
	Examiner	Art Unit	
	JULIE HA	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 August 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-35* is/are pending in the application.

4a) Of the above claim(s) *1-8 and 16-25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *9-15 and 26-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/26/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application.
6) ☐ Other: _____.

DETAILED ACTION

Response to Election/Restriction filed on August 11, 2010 is acknowledged. Claims 1-35 are pending in this application.

Restriction

1. Applicant's election of Group II and the election of species R1, R2 and R3 are COR4 wherein R4 is methyl, coupling agent is HATU, the solvent is DMF, the tertiary amine is NMM, the catalyst is 10% Pd/C in DMF, the acid treatment is HCl, the base treatment is carried out with sodium methoxide in methyl alcohol in the reply filed on August 11, 2010 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

The restriction requirement is deemed proper and is made FINAL in this office action.

Claims 1-8 and 16-25 are hereby withdrawn pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Claims 9-15, 26-35 are examined on the merits in this office action.

TRADEMARK

2. The use of the trademark SEPHADEX® has been noted in this application at paragraph [0077] of instant specification US 2009/0163695 A1. The use of the trademark AMBERLYST® has been noted in this application at paragraph [0096] of

instant specification US 2009/0163695 A1.They should be capitalized wherever they appear and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Objection

3. The abstract is objected to for the following minor informality:

Applicant is reminded of the proper language and format for an abstract of the disclosure.

The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

The language should be clear and concise and should not repeat information given in the title. It should avoid using phrases which can be implied, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc.

In the instant case, the abstract recites, "The present invention relates to a new process carried out entirely in solution, for the preparation in high yields of high purity bicyclic peptide compounds of formula (I)..." is directed to a method..." at lines 1-4 of the abstract. Applicant should correct these informalities. See MPEP 608.01(b). For

example, the abstract should read, "A new process for the preparation of bicyclic peptide compounds in high yields of high purity...is described."

4. Claim 15 is objected for the following reason: Claim 15 depends from claim 9, and recites a method step of claim 1, which has been withdrawn from consideration, as being drawn to nonelected invention. Claim 15 cannot depend from a withdrawn claim. Applicant is required to correct this.

Rejection

35 U.S.C. 112, second paragraph

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 9-15 and 26-35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

7. Claim 9 recites, "...wherein R is a group selected from benzotriazole, possibly substituted with a halogen, azabenzotriazole and succinimidyl..." The phrase "possibly" renders the claim indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention. See MPEP § 2173.05(d). Because claims 10-15 and 26-35 depend from indefinite claim 9 and do not clarify the point of confusion, they must also be rejected under 35 U.S.C. 112, second paragraph.

8. Claim 11 recites, "...phenyl possibly substituted with a halogen atom, benzyl or benzoyl." The phrase "possibly" renders the claim indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention. See

MPEP § 2173.05(d). Because claims 12-13 depend from indefinite claim 11 and do not clarify the point of confusion, they must also be rejected under 35 U.S.C. 112, second paragraph.

9. Claim 26 recites, "...a carbodiimide possibly in combination with a hydroxy derivative, phosphonium salts, N-oxide guanidine salts and uranium salts." The phrase "possibly" renders the claim indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention. See MPEP § 2173.05(d). Because claim 27 depends from indefinite claim 26 and do not clarify the point of confusion, they must also be rejected under 35 U.S.C. 112, second paragraph.

10. Claim 26 recites, "...a carbodiimide possibly in combination with a hydroxy derivative..." it is unclear what modifications are encompassed within a "hydroxy derivative". The specification does not define what modifications are encompassed within a "hydroxy derivative". The dictionary defines a derivative as "a chemical substance derived from another substance either directly or by modification or partial substitution" (see p. 3 of http://cancerweb.ncl.ac.uk/cgi-bin/omd?query-derivative, enclosed). Because claim 27 depends from indefinite claim 26 and do not clarify the point of confusion, they must also be rejected under 35 U.S.C. 112, second paragraph.

35 U.S.C. 112, first paragraph

11. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to

which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12. Claims 9-10, 15, 26, 28-35 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, as of the filing date of the application, of the specific subject matter later claimed by him. The courts have stated:

"To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); *In re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966." Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

The MPEP lists factors that can be used to determine if sufficient evidence of possession has been furnished in the disclosure of the Application. These include "level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient." MPEP 2163.

Further, for a broad generic claim, the specification must provide adequate written description to identify the genus of the claim. In Regents of the University of California v. Eli Lilly & Co., the court stated:

"A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials. Fiers, 984 F.2d at 1171, 25 USPQ2d at 1606; *In re Smythe*, 480 F.2d 1376, 1383, 178 USPQ 279, 284-85 (CCPA 1973) ("In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus. . . ."). Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

The MPEP does state that for generic claim the genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. MPEP 2163. If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. See MPEP 2163. Although the MPEP does not define what constitute a sufficient number of representative, the Courts have indicated what do not constitute a representative number species to adequately describe a broad generic. In Gostelli, the Court determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. *In re Gostelli*, 872 F.2d at 1012, 10 USPQ2d at 1618.

In the instant case, the claims are drawn to a method for preparing a bicyclic glycopeptides compound of formula (I-A) wherein R1, R2 and R3, equal or different from each other, can be hydrogen or an oxygen protecting group, comprising the following steps:...with a suitable coupling agent to obtain a derivative of formula (II-A). Claim 26 is further drawn to "coupling agent is selected from...a carbodiimide possibly in combination with a hydroxy derivative..." The generic statements oxygen protecting

group, suitable coupling agent and hydroxy derivative do not provide ample written description for the compounds since the claims do not describe a single structural feature. The specification does not clearly define or provide examples of what qualify as compounds of the claimed invention.

As stated earlier, the MPEP states that written description for a genus can be achieved by a representative number of species within a broad generic. It is unquestionable claims 9 and 26 are broad generics with respect all possible compounds encompassed by the claims. The possible structural variations are limitless to any class of peptide or a peptide-like molecule or any organic molecule that can function as an oxygen protecting group, any molecule or reagent that can function as a suitable coupling agent, and any compounds that functions as hydroxy derivative. It must not be forgotten that the MPEP states that if a peptide is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP 2163. Here, though the claims may recite some functional characteristics, the claims lack written description because there is no disclosure of a correlation between function and structure of the compounds beyond compounds disclosed in the examples in the specification. Moreover, the specification lack sufficient variety of species to reflect this variance in the genus since the specification does not provide any examples of derivatives. The specification is void of organic molecules that functions as a peptide-like molecule or any small or organic compounds that qualify for the functional

characteristics claimed as an oxygen protecting group, any molecule or reagent that can function as a suitable coupling agent, and other synthetic or small molecules that can function as a hydroxy derivative.

Factors to be considered in making the determination as to whether one skilled in the art would recognize that the applicant was in possession of the claimed invention as a whole at the time of filing include: (a) Actual reduction to practice; (b) Disclosure of drawings or structural chemical formulas; (c) Sufficient relevant identifying characteristics such as: (i) Complete structure, (ii) Partial structure, (iii) Physical and/or chemical properties or (iv) Functional characteristics when coupled with a known or disclosed correlation between function and structure; (d) Method of making the claimed invention; (e) Level of skill and knowledge in the art and (f) Predictability in the art. While all of these factors are considered, a sufficient number for a *prima facie* case are discussed below.

In regards to claim 9, the claim is defined by a functional feature, namely an "oxygen protecting group" and "suitable coupling agent". In regards to claim 26, the claim is defined by a functional feature, namely "hydroxy derivative".

For a broad generic claim, the specification must provide adequate written description to identify the genus of the claim. In *Regents of the University of California v. Eli Lilly & Co.* the court stated that, "A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *Fiers*, 984 F.2d at 1171, 25 USPQ2d

1601; *In re Smythe*, 480 F.2d 1376, 1383, 178 USPQ 279, 284985 (CCPA 1973) ("In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus ...") *Regents of the University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398. MPEP § 2163 states that for a generic claim the genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. Although the MPEP does not define what constitute a sufficient number of representative species, the courts have indicated what do not constitute a representative number of species to adequately describe a broad generic. In *Gostelli*, the courts determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. *In re Gostelli*, 872, F.2d at 1012, 10 USPQ2d at 1618.

The functional features embraced by genus of oxygen protecting group, suitable coupling agent, and hydroxy derivative embraces not only compounds which are structurally close to each other, but also any compounds that are already known to function as oxygen protecting group, coupling agent and hydroxy derivative, but for which that mode of action has not been identified and many compounds yet to be discovered.

The specification discloses that "the activated derivatives can be prepared...numerous known coupling agents, such as isobutyl chloroformate (IBCF), a

carbodiimide…HOBt, HOAt…TNTU or TSTU" (see paragraph [0023] of instant specification US 2009/0163695). The specification discloses that "the term oxygen protecting group…refers to a protecting group selected from those commonly used for the protecting or –OH groups and well known to any person skilled in the art…COR_4 wherein R_4 is a linear or branched alkyl group, with from 1 to 4 carbon atoms, the phenyl being possibly substituted by a halogen atom, benzyl or benzoyl; the oxygen protecting group is preferably acetyl" (see paragraph [0031] of instant specification as described above). The specification discloses that "hydroxy derivative is selected from 1-hydroxybenzotriazole, 6-chloro-1-hydroxybenzotriazole, hydroxysuccinimide and 1-hydroxy-7-azabenzotriazole (see originally filed claim 18). The working examples describe the method of preparation of the bicyclic peptides.

Description of IBCF, carbodiimide, HOBt, HOAt, TNTU or TSTU for coupling agent, acetyl or linear or branched alkyl group for oxygen protecting group, and 1-hydroxybenzotriazole, 6-chloro-1-hydroxybenzotriazole, hydroxysuccinimide and 1-hydroxy-7-azabenzotriazole for hydroxy derivative is not sufficient to encompass numerous other proteins and proteases that belong to the same genus. For example, there are varying lengths, varying amino acid compositions or oxygen protecting group or hydroxy derivative, various components and numerous distinct qualities that make up the genus. There is not sufficient amount of examples provided to encompass the numerous characteristics of the whole genus claimed.

The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention.

See *In re Wilder*, 736 F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate"). Accordingly, it is deemed that the specification fails to provide adequate written description for the genus of the claims and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

Conclusion

13. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JULIE HA whose telephone number is (571)272-5982. The examiner can normally be reached on Mon-Thurs, 5:30 AM to 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Julie Ha/
Primary Examiner, Art Unit 1654